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THOMPSON HINE L.L.P.
Intellectual Property Group
P.O. BOX 8801
DAYTON, OH 45401-8801

EXAMINER	
WANG, CHANG YU	
ART UNIT	**PAPER NUMBER**
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,826	VERFAILLIE ET AL.	
	Examiner	Art Unit	
	Chang-Yu Wang	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/16/08,9/23/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendments filed 8/18/08 and 10/10/08 are acknowledged. Claims 2-3 and 7-8 are amended. Claims 1-13 are pending in this application. Claim 12 is withdrawn with traverse (filed on 11/19/07) from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

2. Claims 1-11 and 13 are under examination with respect to bone marrow and dopaminergic neurons in this office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.

4. Applicant's arguments filed on 8/18/08 and 10/10/08 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on 9/16/08 & 9/23/08 have been considered by the examiner.

Specification

6. The objection to the specification is withdrawn in response to Applicant's amendment to the specification.

Claim Objections

7. The recitation of N2 supplement is a trademark. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections/Objections Maintained

In view of the amendment filed on 8/18/08 and 10/10/08, the following rejections are maintained.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3 and 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is maintained for the reasons of record, and as follows.

On p. 10 of the response, Applicant argues that the rejection is obviated because claim 3 has been amended to delete the trademark symbol. Applicant's argument has been fully considered but it is not persuasive.

In contrast, the recitation of "N2 supplement" is a trademark or trade name. A trademark or trade name is used to identify a source of goods, and not the goods

themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. Thus, claim 3 is indefinite.

In addition, claims 7-8 recite "cells that are not embryonic stem cells, embryonic germ cells or germ cells and can differentiate into at least one cell type of each of the endodermal, ectodermal and mesodermal embryonic lineages". Neither the specification nor the prior defines what cells "that are not embryonic stem cells, embryonic germ cells or germ cells and can differentiate into at least one cell type of each of the endodermal, ectodermal and mesodermal embryonic lineages" are. The metes and bounds of what is encompassed within the definition of cells that are not embryonic stem cells, embryonic germ cells or germ cells and can differentiate into at least one cell type of each of the endodermal, ectodermal and mesodermal embryonic lineages cannot determine. Thus, the claims are indefinite.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-7, 9, 11 and 13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO02/086073 (Studer et al., published Oct 31, 2002, cited in office action mailed 10/18/07) in view of US2003/0211605 (Lee et al., published Nov 13, 2003, priority May 1, 2000). The rejection is maintained for the reasons made of record.

On p. 11-12 of the response, Applicant argues that there is no motivation to combine even if there were motivation to combine, the combination would not result in the claimed invention. On p. 11-12 of the response, Applicant argues that the claimed invention requires the sequential steps of culturing stem cells with neurotrophic factors and co-culturing the cells with astrocytes but Studer teaches culturing stem cells supplemented with bFGF, SHH and FGF8 at the same time and also teaches culturing ES cells to generate astrocytes not co-culturing. On p. 13-14 of the response, Applicant

argues that Lee does not compensate for the deficiencies of Studer because Lee teaches culturing ES cells with bFGF, SHH or FGF8 and optionally with BDNF and teaches using astrocytes in neuronal cell culture but does not teach sequential culturing stem cells first with bFGF, then with FGF8 and SHH , then with BDNF, and finally co-culturing the cells with astrocytes. Applicant's arguments have been fully considered but they are not persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. MPEP. §2144.07.

Specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involve not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See *CTS Corp. v. Electro Materials Corp. of America* 202 USPQ 22 (DC SNY 1979); and *In re Burckel* 201 USPQ 67 (CCPA 1979).

It is not necessary that the claimed invention be expressly suggested in any one or all of the references to justify combining their teachings; rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Only a reason, suggestion or motivation need appear in the cited prior art in order to combine references under 35 U.S.C. 103. *Pro Mold Tool Col. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

Further, there is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." *Motorola, Inc. v. Interdiqital Tech. Corp.,* 43 USPQ2d 1481, 1489 (Fed. Cir. 1997). See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In contrast, the combined references do render the claimed invention obvious. Although the instant method recites adding bFGF, FGF8, SHH, BDNF sequentially, at the end of the final steps, the culture medium contains the identical growth factors as those in Studers to induce neuronal differentiation. By adding bFGF, FGF8, SHH and BDNF in a different order from that of Studer's method would not result in any superior result because at the end the culture medium still contains the same growth factors and the same cultured ES cells, which will be induced to differentiate into neurons. The

specification fails to show that adding these growth factors sequentially in the Studer's culture medium would result in any unexpected result such as different neuronal populations or enhancing neuronal differentiation because the result of adding bFGF, FGF8, SHH and BDNF are expected.

In addition, although Studer does not explicitly teach co-culturing astrocytes, the cell culture of Studer is a cell mixture, which encompasses astrocytes and thus meets the limitation of co-culturing cells with astrocytes. In addition, it is known in the art that neuronal cultures require astrocytes to maintain and support neuronal survival and differentiation because the mixture of neuronal stem or progenitor cells to differentiate into neurons encompass cells to differentiate into astrocytes. Further, it is known in the art and is a standard procedure to culture neuronal progenitor cells or neural stem cells with astrocytes to maintain or enhance neuronal survival as evidenced by Walsh et al. (Neurosci. Lett 1992. 138: 103, abstract). Note that

"The selection of a known material based on its suitability for its intended use supported a *prima facie* obviousness determination in *Sinclair & Carroll Co. v. Interchemical Corp.*, 325 U.S. 327, 65 USPQ 297 (1945)." See MPEP 2144.07

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105USPQ 233, 235 (CCPA 1955)" See MPEP 2144.05-II

In addition,

"It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980); see also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992). See MPEP § 2144.06.

8. Claims 1-11 and 13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO02/086073 (Studer et al., published Oct 31, 2002, cited in office action mailed 10/18/07) in view of US2003/0211605 (Lee et al., published Nov 13, 2003, priority May 1, 2000) as applied to claims 1-7, 9, 11 and 13 above, and further in view of Song et al. (Methods in Mol. Biol. 2002. 198: 79-88). The rejection is maintained for the reasons made of record.

On p. 15-16 of the response, Applicant argues that Song does not cure the deficiencies of Suder and Lee to reach the claimed invention. Applicant's arguments have been fully considered but they are not persuasive.

In contrast, as previously made of record and for the reasons as set forth above, Studer and Lee do render the claimed invention of the claims 1-7, 9, 11 and 13 obvious. Although Studer and Lee do not teach multipotent adult progenitor cells and bone marrow as recited in instant claims 7-10, Song et al. teach a method of culturing and differentiating bone marrow and umbilical cord blood cells into neural progenitor cells and neurons in a DMEM/F12 medium comprising FGF-2/bFGF, EGF, transferrin, insulin, putrescine, progesterone, selenium, trans-retinoic acid, BDNF and NGF (see p. 80, in p articular). Song et al. also teach culturing human and mouse bone marrow and human umbilical cord cultures (p. 82-83). The bone marrow and umbilical cord blood cells encompass stem cells and nonhematopoietic progenitor cells from bone marrow are mesenchymal stem cells or bone marrow stromal cells as taught by Song et al. (p.79), which meet the limitations of multipotent adult progenitor cells (MAPCs) and bone marrow as recited in instant claims 7-10. Thus, it is obvious to to differentiate stem

cells that are derived from multipotent adult progenitor cells (MAPCs) and bone marrow into neurons by using the culture conditions of WO02/086073 and US2003/0211605.

New Grounds of Rejection Necessitated by the Amendment

The following rejections are new grounds of rejections necessitated by the amendment filed on 8/18/08 and 10/10/08.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims 7-8 as amended are directed to a method for inducing stem cells to differentiate into neurons wherein the stem cells are selected from the group consisting of neural stem cells, embryonic germ cells, embryonic stem cells, and cells that are not embryonic stem cells, embryonic germ cells, or germ cells and can differentiate into at least one cell type of each of the endodermal, ectodermal and mesodermal embryonic

lineages. The instant claims now recite the limitation of "cells that are not embryonic stem cells, embryonic germ cells, or germ cells and can differentiate into at least one cell type of each of the endodermal, ectodermal and mesodermal embryonic lineages", which was not clearly disclosed in the specification and claims as filed, and now change the scope of the instant disclosure as filed. Such limitation recited in the present claims, which did not appear in the specification or original claims, as filed, introduces new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

The specification fails to disclose the above underlined limitation. Accordingly, in the absence of sufficient recitation of such limitation, the specification does not provide adequate written description to support the complement immunoreactivant as recited in claims 7-8. Thus the recitation constitutes new matter absent evidence for their support. Applicant is required to cancel the new matter in the reply to this office action. Alternatively, Applicant is invited to clearly point out the written support for the instant limitations.

Conclusion

10. NO CLAIM IS ALLOWED.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
December 15, 2008

/Christine J Saoud/
Primary Examiner, Art Unit 1647